

CLAIMS

1. A polypeptide derivable from human NESP55 wherein the said polypeptide is derivable, or predicted from the amino acid sequence of human NESP55 to be derivable, by endoproteolytic cleavage of a polypeptide having the amino acid sequence

IRLEVPKRMDRRSRAQQWRRARHNYNDLCPPIGRRAATALLWLSCSIALLRAL  
ATSNARAQQRAAAQQRSSFLNAHHRSGAQVFPESPESEDHEHEEADLELSLP  
ECLEYEEEFDYETESETESIIESETDFETEPETAPTTEPETEPEDDRGPVVPK  
HSTFGQSLTQRLHALKLRS PDASPSRAPPSTQEPQSPREGEELKPEDKDPRRD  
PEESKEPKEEKQRRRCKPKKPTRRDASPESSKKGPIPIRRH

or

MDRRSRAQQWRRARHNYNDLCPPIGRRAATALLWLSCSIALLRALATSNARAQ  
QRAAAQQRSSFLNAHHRSGAQVFPESPESEDHEHEEADLELSLPECLEYEEE  
FDYETESETESIIESETDFETEPETAPTTEPETEPEDDRGPVVPKHSTFGQSL  
TQRLHALKLRS PDASPSRAPPSTQEPQSPREGEELKPEDKDPRRDPEESKEPK  
EEKQRRRCKPKKPTRRDASPESSKKGPIPIRRH

(human NESP55) or of a variant thereof, wherein the polypeptide variant has an amino acid sequence which has at least 90% identity with the amino acid sequence given above.

2. The polypeptide of Claim 1 wherein the N-terminal amino acid residue of the said processed polypeptide is immediately preceded in the amino acid sequence of human NESP55 by two consecutive basic amino acid residues or by a basic amino acid residue.

3. The polypeptide of Claim 1 or Claim 2 wherein the C-terminus of the said processed polypeptide is immediately preceded by two consecutive basic amino acid residues or by a basic amino acid residue.

4. The polypeptide of any one of Claims 1 to 3 comprising the amino acid sequence LHAL or the amino acid sequence GPIPIRRH.
5. The polypeptide according to any one of Claims 1 to 4 consisting of the amino acid sequence LHAL or the amino acid sequence GPIPIRRH.
6. A polypeptide consisting of the amino acid sequence  $X_n$ LHAL $Z_m$ , or  $X_n$ GPIPIRRH $Z_m$  wherein  $X_n$  represents the amino acid sequence of the consecutive  $n$  amino acids immediately N terminal to the amino acid sequence LHAL or GPIPIRRH and wherein  $Z_m$  represents the amino acid sequence of the consecutive  $m$  amino acids immediately C terminal to the amino acid sequence LHAL or GPIPIRRH, wherein  $n$  and  $m$  may independently be any number between 0 and 30 amino acids.
7. A polypeptide according to Claim 6 wherein one or both of  $X_n$  or  $Z_m$  consists of the sequence immediately flanking the LHAL or GPIPIRRH sequences in native human NESP55.
8. A polypeptide variant, fragment, derivative or fusion of a polypeptide having the amino acid sequence

IRLEVPKRMDRRSRAQQWRRARHNYNDLCPPIGRRAATALLWLSCSIALLRAL  
 ATSNARAQQRAAAQQRSSFLNAHHRSGAQVFPESPESEDHEHEEADLELSLP  
 ECLEYEEEFDYETESETESIESETDFETEPETAPTTEPETEPEDDRGPVVPK  
 HSTFGQSLTQRLHALKLRSPDASPSRAPPSTQEPQSPREGEELKPEDKDPRRD  
 PEESKEPKKEKQRRRCKPKKPTRRDASPEPSKKGPIPIRRH

or a fusion of a said variant or fragment or derivative, wherein the polypeptide variant has an amino acid sequence which has at least 90% identity with the amino acid sequence given above and wherein the said polypeptide variant, derivative, fragment or fusion does not have the amino acid sequence

MDRRSRAQQWRRARHNYNDLCPPIGRRAATALLWLSCSIALLRALATSNARAQ  
 QRAAAQQRSSFLNAHHRSGAQVFPESPESEDHEHEEADLELSLPECLEYEEE  
 FDYETESETESIESETDFETEPETAPTTEPETEPEDDRGPVVPKHSTFGQSL  
 TQRLHALKLRSPDASPSRAPPSTQEPQSPREGEELKPEDKDPRDPEESKEPKE  
 EKQRRRCKPKKPTRRDASPEPSKKGPIPIRRH.

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9. A recombinant polynucleotide encoding or complementary to a polynucleotide encoding a polypeptide, for example a fusion polypeptide, according to any one of Claims 1 to 8.

10. A recombinant polynucleotide suitable for expressing a polypeptide according to any one of Claims 1 to 8.

11. A polynucleotide vector construct comprising a polynucleotide according to Claim 9 or 10.

12. A host cell transformed with a polynucleotide vector construct according to Claim 11.

13. A method of making a polypeptide as defined in any one of claims 1 to 8 the method comprising culturing a host cell according to Claim 12 and isolating said polypeptide from said host cell.

14. A polypeptide obtainable by the method of Claim 13.

15. An antibody reactive towards a polypeptide according to any one of Claims 1 to 8 or having an amino acid sequence given in claim 1.

16. An antibody according to Claim 15 or an antibody reactive towards the peptide sequence GAIPPIRRH for use in medicine.

17. A polypeptide according to any one of Claims 1 to 8 or a polypeptide having an amino acid sequence given in claim 1 (human NESP55) for use in medicine.

18. A polynucleotide according to any one of Claims 9 to 11 or a recombinant polynucleotide encoding or complementary to a polynucleotide encoding, and/or suitable for expressing, a polypeptide having an amino acid sequence given in claim 1, for use in medicine.

19. A pharmaceutical composition comprising an antibody as defined in Claim 15 or 16 or a polypeptide as defined in Claim 17 or a polynucleotide as defined in Claim 18 or an antagonist as defined in Claim 26 or 27 and a pharmaceutically acceptable carrier.

20. A method of treating or preventing obesity in a patient, the method comprising administering to the patient an effective amount of an antibody as defined in Claim 15 or 16, a polypeptide as defined in Claim 17 or polynucleotide as defined in Claim 18 or an antagonist as defined in Claim 26 or 27.

21. The use of an antibody as defined in Claim 15 or 16 or a polypeptide as defined in Claim 17 or polynucleotide as defined in Claim 18 or an antagonist as defined in Claim 26 or 27 in the manufacture of a medicament for the treatment of obesity.

22. A method of identifying a polypeptide (interacting polypeptide) that is capable of interacting with a polypeptide as defined in claim 17, or that is capable of interacting with a polypeptide containing the sequence GAIPRRH, the method comprising the steps of (1) exposing the said polypeptide to a test composition that may comprise a said interacting polypeptide, (2) detecting an interaction between the said polypeptide and a said interacting polypeptide and optionally (3) identifying and/or isolating the said interacting polypeptide.

23. A substantially pure interacting polypeptide identified or identifiable by the method according to Claim 24.

24. The interacting polypeptide of Claim 23 wherein the interacting polypeptide is a receptor.

25. A nucleic acid encoding the interacting polypeptide according to Claim 23 or 24.

26. An antagonist of the interacting polypeptide as defined in any one of Claim 23 and 24.

27. An antagonist according to Claim 26 which is an antibody.

28. An antagonist as defined in Claim 26 or 27 for use in medicine.

29. A method of identifying a compound capable of disrupting or preventing the interaction between a polypeptide as defined in claim 17 or a GAIPRRH-containing polypeptide and an interacting polypeptide according to Claim 23 or 24 wherein the polypeptide as defined in claim 17 or the GAIPRRH-containing

polypeptide and/or an interacting polypeptide according to Claim 23 or 24 are exposed to the said compound and the interaction between the polypeptide as defined in claim 17 or the GAIPRRH-containing polypeptide and an interacting polypeptide according to Claim 23 or 24 is measured in the presence and absence of the compound.

30. A method of identifying a compound capable of binding to an interacting polypeptide according to Claim 23 or 24 wherein the ability of the compound to bind to the said interacting polypeptide is measured.

31. A kit of parts comprising a polypeptide as defined in claim 17 and an interacting polypeptide according to Claim 23 or 24.

32. A compound identified by or identifiable by the method of Claim 29 or 30.

33. A method of disrupting or preventing the interaction between a polypeptide as defined in claim 17 and an interacting polypeptide according to Claim 23 or 24 wherein the said interacting polypeptide or polypeptide as defined in claim 17 is exposed to a compound according to Claim 32 or an antibody according to Claim 15.

34. A compound according to Claim 32 for use in medicine.

35. An interacting polypeptide according to Claim 23 or 24 for use in medicine.

36. A method of determining whether an individual is likely to become or remain obese or become more obese comprising determining the level of NESP55 or a fragment derived or derivable from NESP55 or determining the level of a messenger RNA encoding NESP55, or the activity of NESP55 in a tissue sample, for example a body fluid, and determining that the said level or activity differs from a level or activity found in an individual that is not obese and/or not expected to become obese.

37. A kit of parts for determining whether an individual is likely to become or remain obese or become more obese the kit comprising means to determine the level of NESP55 or a fragment derived or derivable from NESP55 or means to determine the level of mRNA encoding NESP55.

38. The use of an inhibitor of a polypeptide that is capable of cleaving NESP55 in the manufacture of a medicament for treating or preventing obesity.
39. A method of treating or preventing obesity in a patient, the method comprising administering to the patient an effective amount of an inhibitor of a polypeptide that is capable of cleaving NESP55.
40. A compound capable of altering the expression of NESP55.
41. A compound capable of altering the expression of NESP55 for use in medicine.
42. The use of a compound capable of altering the expression of NESP55 in the manufacture of a medicament for the treatment or prevention of obesity.
43. A method of treating or preventing obesity in a patient, the method comprising administering to the patient an effective amount of a compound capable of altering the expression of NESP55.
44. A method of identifying a compound capable of disrupting or preventing the interaction between the peptide LHAL and human 5HT<sub>1B/1D</sub> receptor wherein the LHAL-containing polypeptide and/or the said receptor are exposed to the said compound and the interaction between the polypeptide and the receptor is measured in the presence and absence of the compound.
45. A method of identifying a compound capable of binding to human 5HT<sub>1B/1D</sub> receptor wherein the ability of the compound to bind to the said interacting polypeptide is measured.
46. A kit of parts comprising a LHAL-containing peptide and human 5HT<sub>1B/1D</sub> receptor.
47. A compound identified by or identifiable by the method of Claim 44 or 45.
48. An antibody which reacts with human 5HT<sub>1B/1D</sub> receptor for use in medicine.
49. A method of disrupting or preventing the interaction between the peptide LHAL and human 5HT<sub>1B/1D</sub> receptor the method comprising exposing the human

5HT<sub>1B/1D</sub> receptor to a compound according to Claim 47 or an antibody as defined in Claim 48 or an antibody reactive against the peptide sequence LHAL.

50. A method of treating or preventing obesity in a patient, the method comprising administering to the patient an effective amount of a compound according to Claim 47 or an antagonist of human 5HT<sub>1B/1D</sub> receptor or an antibody reactive against the peptide sequence LHAL.

51. A method according to Claim 50 wherein the human 5HT<sub>1B/1D</sub> receptor antagonist is an anti-receptor antibody.

52. Use of an antagonist of human 5HT<sub>1B/1D</sub> receptor or a compound according to Claim 47 or an antibody reactive against the peptide sequence LHAL in the manufacture of a medicament for treating or preventing obesity.

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